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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/499,526	02/10/2000	Kuanghai Lu	CIBT-P01-058	1398
28120	7590	10/17/2005	EXAMINER	
FISH & NEAVE IP GROUP ROPES & GRAY LLP ONE INTERNATIONAL PLACE BOSTON, MA 02110-2624			DEBERRY, REGINA M	
			ART UNIT	PAPER NUMBER
			1647	

DATE MAILED: 10/17/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

Application No.

09/499,526

Applicant(s)

LU ET AL.

Examiner

Regina M. DeBerry

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 21 September 2005.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) See Continuation Sheet is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) See Continuation Sheet is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- ☐ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date 7/05, 9/05.
- ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_.
- ☐ Notice of Informal Patent Application (PTO-152)
- ☐ Other: \_\_\_\_\_.

***Status of Application, Amendments and/or Claims***

The amendment filed 25 July 2005 has been entered in full. Claims 25-27, 35-37, 52, 55, 56, 61, 62, 65-67, 69-71, 73-75, 79-84, 86, and 113-115 were cancelled. New claims 124-130 were added. Claims 13, 15-21, 23, 28-33, 39, 45, 46, 50, 53, 54, 57-60, 76-78, 85, 87-94, 96-98, 100-112, 116-130 are under examination.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

***Information Disclosure Statement***

The information disclosure statement(s)(IDS) filed 25 July 2005 and 21 September 2005 were received and comply with the provisions of 37 CFR §§1.97 and 1.98. They have been placed in the application file and the information referred to therein has been considered as to the merits. However, some of the references lack a publication date. They are not fully in compliance with 37 CFR 1.97. They will be considered, but will not be printed on the face of the patent issuing from this application.

***Withdrawn Objections And/Or Rejections***

The rejection to claims 13, 21, 23, 33, 45, 87, 92, 93 and 122 under 35 U.S.C. 112, second paragraph, as set forth at pages 6-7 of the previous Office Action (22 March 2005) is *withdrawn* in view of the amendment (25 July 2005).

The rejection to claims 23, 89, 102-105, 108, 111 and 118 under 35 U.S.C. 102(b) as being anticipated by Morley *et al.*, Life Sciences, Vol. 41, pg 2157-2165 (1987), as set forth at pages 7-8 of the previous Office Action (22 March 2005) is *withdrawn* in view of Applicant's arguments (25 July 2005).

**Claim Rejections - 35 USC § 112, First Paragraph, Enablement**

Claims 109, 112, and 119 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The basis for this rejection is set forth at pages 3-4 of the previous Office Action (22 March 2005).

Applicant reiterates the Examiner's rejection from the previous Office Action. Applicant argues that they have provided considerable direction and guidance and have presented working examples such that it is well within the level of ordinary skill in the art to practice the claimed invention without undue experimentation. Applicant cites the specification and Randle (reference submitted in the IDS). Applicant states that the skilled artisan would recognize that such ability to enhance glucose responsiveness in cells would also be useful in treating related conditions such as hyperlipidemia and hyperlipoproteinemia in subjects having altered glucose metabolism. Applicant states that the Examiner has not provided any evidence that the results of the effects of PYY in

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a Zucker Diabetic Fatty rat are not applicable to treating hyperlipidemia or hyperlipoproteinemia.

Applicant's arguments have been fully considered but are not deemed persuasive. The pages in the specification cited by Applicant are prophetic teachings. Exhibit C presented by Applicant demonstrates the effects of PYY in a Zucker Diabetic Fatty rat. Exhibit C demonstrated that PYY **regulated the glucose level** in rats (Emphasis added). The specification and Exhibit C failed to demonstrate a reduction in plasma free fatty acid (FFA) concentrations upon PYY administration (demonstrating PYY stimulates lipolysis). As was stated in the previous Office Action, hyperlipidemia or hyperlipoproteinemia is defined as elevated concentrations of any or all of the lipids in the plasma, such as cholesterol, triglycerides and lipoproteins. The Examiner does not deny an association between glucose metabolism and lipid metabolism. However, an association between glucose metabolism and lipid metabolism **does not mean that PYY regulates lipolysis, thus effecting FFA levels** (Emphasis added). The skilled artisan would recognize that there are many anti-diabetic treatments and drugs to ameliorate complications. Some drugs are insulin-sensitizing agents, while others promote weight loss, increase lipolysis or decrease FFA levels. The instant specification fails to demonstrate that PYY affects hyperlipidemia or hyperlipoproteinemia.

The scientific reasoning and evidence as a whole indicates that the rejection should be maintained.

**Claim Rejections - 35 USC § 112, First Paragraph, Scope of Enablement**

Claims 13, 15-21, 23, 28-33, 39, 45, 46, 50, 53, 54, 57-60, 76-78, 85, 87-94, 96-98, 100-112, 116-130 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for:

the instant methods, "...wherein said PYY agonist or biologically active fragment thereof binds a PYY receptor **AND** promotes glucose-responsiveness of pancreatic islets or pancreatic cells".

does not reasonably provide enablement for:

the instant methods, "...wherein said PYY agonist or biologically active fragment thereof binds a PYY receptor **OR** promotes glucose-responsiveness of pancreatic islets or pancreatic cells".

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. The basis for this rejection is set forth at pages 3-4 of the previous Office Action (22 March 2005).

Applicant states that they have provided direction and guidance and have presented working examples. Applicant argues that the specification discusses PYY agonists and biologically active fragments. Applicant argues that the skilled artisan is well-aware of PYY receptors and methods for determining receptor binding. Applicant cites Gehlert (reference cited in the IDS). Applicant argues that Gehlert provides a summary of some of the knowledge the skilled artisan possesses of PP family receptors and their affinity for PP family member proteins. Applicant maintains that the teachings of the present specification taken in combination with the knowledge of those skilled in

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the art, the specification provides adequate guidance regarding the identification of PYY peptides, agonists and biologically active fragments thereof that bind to a PYY receptor for use in the claimed methods.

Applicant's arguments have been fully considered but are not deemed persuasive. The instant claims read on PYY agonists or biologically active fragments thereof having **only one of the recited functions of PYY** (Emphasis added). Some of the instant claims encompass variants because the PYY agonists and fragments thereof are identified by hybridization to a nucleic acid comprising SEQ ID NO:1 under the specific hybridization conditions set forth in the claims. Other claims encompass variants because they recite fragments of PYY or polypeptides with various percent identities to SEQ ID NO:3. The skilled artisan would recognize that mutations could unpredictably alter activity. References have been cited by the Examiner demonstrating this (see previous Office Actions). The instant methods are drawn to inducing/enhancing the glucose-responsiveness or maintaining/restoring normal pancreatic function to impaired glucose responsive cells. To be fully enabled, the PYY agonist or biologically active fragment thereof **must have the PYY functions of binding a PYY receptor and promoting glucose-responsiveness of pancreatic cells** (Emphasis added).

The scientific reasoning and evidence as a whole indicates that the rejection should be maintained.

**NEW REJECTIONS:**

### **Claim Rejections - 35 USC § 103**

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 23, 89, 102-105, 108, 111 and 118 are rejected under 35 U.S.C. 103(a) as being unpatentable over Morley *et al.*, Life Sciences, Vol. 41, pg 2157-2165 (1987) (cited in the previous Office Action).

The instant claims are drawn to a method for treating a disease associated with altered glucose metabolism, comprising administering to an animal having a disease associated with altered glucose metabolism, an amount of a composition comprising PYY (or PYY agonist or biologically fragment thereof) wherein said disease is obesity.

Morley *et al.* teach the administration of PYY to mice (page 2158, last paragraph). Morley *et al.* teach that the peripheral administration of peptide YY (PYY)



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caused weight loss (abstract; page 2158 last paragraph and Table 5). Morley *et al.* state that neurotransmitters that enhance feeding centrally cause weight loss when given peripherally. Morley *et al.* state that this is best demonstrated in this study where PYY caused weight loss. Morley *et al.* teach that PYY have been shown to produce weight gain after central administration, yet peripherally, PYY caused weight loss, without altering food intake (page 2163, last paragraph-page 2164, first paragraph). Lastly, obesity is a disease that is associated with altered glucose metabolism as evidenced by Vanhala *et al.*, International Journal of Obesity, Vol. 22 369-374, (1998).

Morley *et al.* do not teach the administration of PYY to obese mice. However it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method of Morley *et al.* by administering PYY to obese mice to treat a disease associated with altered glucose metabolism, wherein said disease is obesity. The motivation and expected success is provided by Morley *et al.* in that Morley *et al.* teach that PYY caused weight loss, without altering food intake. An obese patient would have the ability to loss weight without missing important nutrients and vitamins, which would occur with restrictive food intake.

#### **Claim Rejections - 35 USC § 112, Second Paragraph**

Claims 13, 21, 87, 88, 93, 94 and 102 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

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Claims 13, 21, 87, 88, 93 and 94 are drawn to methods directed at impaired pancreatic cells or animals having a disease associated with abnormal glucose metabolism (recited in the preamble of the claim). However, the instant claims recite the limitation "the pancreatic cell" or "the animal" (recited in the body of the claim). Amending the instant claims to recite "said pancreatic cell" or "said animal" would be remedial.

Claim 102 is indefinite because it fails to teach the *dose effective* to treat a disease associated with altered glucose metabolism. Thus the claim, as recited, reads on administering trace amounts of PYY instead of dosages of PYY that are effective to achieve the goal recited in the preamble.


### ***Conclusion***


No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Regina M. DeBerry whose telephone number is (571) 272-0882. The examiner can normally be reached on 9:00 a.m.-6:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda G. Brumback can be reached on (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

  
RMD  
10/12/05

  
JOSEPH MURPHY  
PATENT EXAMINER

Continuation of Disposition of Claims: Claims pending in the application are 13,15-21,23,28-33,39,45,46,50,53,54,57-60,76-78,85,87-94,96-98,100-112 and 116-130.

Continuation of Disposition of Claims: Claims rejected are 13,15-21,23,28-33,39,45,46,50,53,54,57-60,76-78,85,87-94,96-98,100-112 and 116-130.